REMARKS

Courtesies extended to Applicants' representative in the personal interview held August 7, 2002, are acknowledged with appreciation.

As discussed at the personal interview, the present invention relates to co-repressor polypeptides that are capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors. Exemplary members of the silencing mediators of retinoic acid and thyroid hormone receptors (SMRT) are provided, including various isoforms of human, mouse and Drosophilla SMRT co-repressor.

Claims 1 and 3-37 were pending before this communication. By this response, claims 3-6, 9, 10, 12-14, 16-19, and 21-23 have been amended, and claim 38 has been added to define Applicant's invention with greater particularity. For the Examiner's convenience, a marked up version of claims reflecting these amendments is provided herewith as APPENDIX A. These amendments add no new matter as they are fully supported by the specification and original claims. It is respectfully submitted that the amendments submitted herewith place the application in condition for allowance, or at a minimum, in better condition for appeal. Accordingly, entry of the proposed amendments is respectfully requested.

In view of the above amendments, claims 1, 8, 11 and 15 have been cancelled, as have non-elected claims 26-37, without prejudice. Accordingly, claims 3-7, 9, 10, 12-14, 16-25 and 38 will be pending upon entry of the amendments submitted herewith. For the Examiner's convenience, a complete set of the pending claims is provided in APPENDIX B.

The Examiner's observation that the signature of Inventor Chen is missing from the declaration is noted. This informality will be addressed in due course under separate cover.

The Examiner's acknowledgement that replacement drawings submitted for Figures 4, 6C and 12C are acc ptable is noted with appreciation. With respect to the repeated objection to Figures 5A and 9, replacement sheets for these drawings are provided herewith. Accordingly, reconsideration and withdrawal of this objection are respectfully requested.

The rejections of claims 1, 3, 5, 6, 8, 11, 16 and 19-22 (and claims 4, 7, 9, 10 and 12) under 35 U.S.C. 112, first paragraph, as allegedly lacking sufficient written description, is respectfully traversed. As discussed at the personal interview, Applicants have amended the claims so that each independent claim defines the claimed polynucleotide with reference to both structure and function. Thus, for example, claim 4 contemplates nucleic acid encoding a co-repressor which mediates transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily and has the amino acid sequence set forth in SEQ ID No. 5, or conservative variations thereof. As discussed at the personal interview, the terminology employed in this claim is fully consistent with the allowed claims of Parent Application Serial No. 08/522,726. Moreover, the terminology employed in this claim embraces those changes which would be least likely to impact the structure or function of the resulting polypeptide. Accordingly, based on the widely accepted usage of the terminology "conservative variation", it is respectfully submitted that the disclosure clearly provides written description for the claimed subject matter.

Similarly, claim 5 contemplates nucleic acid encoding a co-repressor which mediates transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily, wherein the polynucleotide hybridizes under stringent conditions to SEQ ID No. 4. Since this claim makes reference to a specific target sequence, and merely contemplates sequences which hybridize thereto under stringent conditions, it is respectfully submitted that ample written description has been provided to support this claim.

Claim 6 also defines the claimed subject matter with reference to both structure and function, requiring nucleic acid which encodes a co-repressor which mediates

transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily, wherein th co-repressor has a high degre of sequence identity with SEQ ID No. 5. Thus, this claim also makes explicit reference to a specific sequence and merely contemplates a limited amount of variation therefrom. It is respectfully submitted that this claim also is fully supported by the disclosure.

Consistent with amendments to claim 4 submitted herewith, claims 9 and 12 have similarly been rewritten as independent claims, with reference to SEQ ID Nos. 7 and 9, respectively. Thus, these claims specifically require nucleic acid encoding a co-repressor which mediates transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily and having a defined amino acid sequence, or conservative variations thereof. Based on the widely accepted usage of the terminology, "conservative variation", it is respectfully submitted that the disclosure clearly provides written description for the claimed subject matter.

The rejection of claims 3, 5 and 16 under 35 U.S.C. 112, second paragraph, as allegedly being indefinite, is respectfully traversed. As discussed at the personal interview, "hybridizing under stringent conditions" is respectfully submitted to be clear to those of skill in the art. Moreover, it is respectfully submitted that specific hybridization conditions need not be recited since Applicants' specification provides ample guidance as to the scope intended for these claims. See, for example, page 17, lines 6-9, where it is indicated that a polynucleotide which hybridizes, preferably under high stringency conditions, will typically have at least 80% sequence identity with the polynucleotides described in Applicants' specification.

The rejection of claims 9 and 10 under 35 U.S.C. 112, second paragraph, as allegedly being indefinite, is respectfully traversed. Applicants respectfully disagree with the Examiner's assertion that the phrase "substantially the same" is not defined in the specification (see the last two lines at page 7 of the Office Action). Contrary to the Examiner's assertion, this terminology is expressly defined at page 17, line 30 through page 18, line 14 of Applicant's specification.

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In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved in view of this communication, the Examiner is encouraged to call the undersigned so that a prompt disposition of this Application can be achieved.

Respectfully submitted,

Date 9/3/02

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Enclosures----APPENDICES A & B
Proposed replacement Figures 5A and 9

APPENDIX A
Marked up version of the amended claims showing changes made

3. (Amended) The polynucleotide of claim ~~[1]~~ 4 and polynucleotides that hybridize thereto under stringent conditions, wherein the SMRT co-repressor comprises a repression domain having

a) less than about 83% identity with a Sin3A interaction domain of N-CoR set forth as amino acids 255 to 312 of SEQ ID NO: 11;

b) less than about 57% identity with repression domain 1 of N-CoR set forth as amino acids 1 to 312 of SEQ ID NO: 11;

c) less than about 66% identity with a SANT domain of N-CoR set forth as amino acids 312 to 668 of SEQ ID NO: 11; or

d) less than about 30% identity with repression domain 2 of N-CoR set forth as amino acids 736 to 1031 of SEQ ID NO: 11.

4. (Amended) ~~[The]~~ An isolated polynucleotide ~~[of claim 1,]~~ encoding a member of a family of silencing mediators of retinoic acid receptor and thyroid hormone receptor (SMRT), or an isoform or peptide portion thereof (collectively, a SMRT co-repressor), or an isolated polynucleotide complementary thereto, wherein said SMRT co-repressor is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors, and wherein the SMRT co-repressor ~~[is a human SMRT co-repressor having]~~ comprises an amino acid sequence as set forth in SEQ ID NO: 5 or conservative variations thereof.

5. (Amended) ~~[A]~~ An isolated polynucleotide ~~[of claim 1, which]~~ encoding a member of a family of silencing mediators of retinoic acid receptor and thyroid hormone receptor (SMRT), or an isoform or peptide portion thereof (collectively, a SMRT co-repressor), or an isolated polynucleotide complementary thereto, wherein said SMRT co-repressor is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors, and wherein said co-repressor is

encoded by a polynucleotide which hybridizes under stringent conditions with SEQ ID NO:~~[5]~~ 4.

6. (Amended) ~~[A]~~ An isolated polynucleotide ~~[of claim 1, which]~~ encoding a member of a family of silencing mediators of retinoic acid receptor and thyroid hormone receptor (SMRT), or an isoform or peptide portion thereof (collectively, a SMRT co-repressor), or an isolated polynucleotide complementary thereto, wherein said SMRT co-repressor is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors, wherein said co-repressor has at least 80% sequence identity with SEQ ID NO:5.

9. (Amended) ~~[The]~~ An isolated polynucleotide ~~[of claim 8,]~~ encoding a member of a family of silencing mediators of retinoic acid receptor and thyroid hormone receptor (SMRT), or an isoform or peptide portion thereof (collectively, a SMRT co-repressor), or an isolated polynucleotide complementary thereto, wherein said SMRT co-repressor is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors, and wherein said polynucleotide encodes a polypeptide having ~~[substantially]~~ the ~~[same]~~ amino acid sequence ~~[as]~~ set forth in SEQ ID NO: 7 or conservative variations thereof.

10. (Amended) The polynucleotide of claim ~~[8]~~ 9, which has a nucleotide sequence substantially the same as set forth in SEQ ID NO: 6.

12. (Amended) ~~[The]~~ An isolated polynucleotide ~~[of claim 11,]~~ encoding a member of a family of silencing mediators of retinoic acid receptor and thyroid hormone receptor (SMRT), or an isoform or peptide portion thereof (collectively, a SMRT co-repressor), or an isolated polynucleotide complementary thereto, wherein said SMRT co-repressor is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors, and wherein said polynucleotide encodes a polypeptide having ~~[substantially]~~ the ~~[same]~~ amino acid sequence ~~[as]~~ set forth in SEQ ID NO: 9 or conservative variations thereof.

13. (Amended) The polynucleotide of claim ~~[11]~~ 12, which has a nucleotide sequence substantially the same as set forth in SEQ ID NO: 8.

14. (Amended) ~~[The]~~ An isolated polynucleotide ~~[of claim 1,]~~ encoding a member of a family of silencing mediators of retinoic acid receptor and thyroid hormone receptor (SMRT), or an isoform or peptide portion thereof (collectively, a SMRT co-repressor), or an isolated polynucleotide complementary thereto, wherein said SMRT co-repressor is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors, and wherein said polynucleotide comprises a nucleotide sequence having at least 80% sequence identity with a polynucleotide selected from the group consisting of:

(a) nucleotides 1 to 3094 of SEQ ID NO: 4;

(b) nucleotides 1 to 3718 of SEQ ID NO: 6;

(c) nucleotides 1 to 2801 of SEQ ID NO: 8; and

(d) polynucleotides hybridizing under stringent conditions to (a), (b), or (c),

provided that the polynucleotide does not contain a sequence identical to SEQ ID NO: 11.

16. (Amended) A polynucleotide ~~[that has at least 80% sequence identity with a polynucleotide]~~ according to claim 14, ~~[provided that the polynucleotide does not contain a sequence identical to SEQ ID NO: 11]~~, wherein said polynucleotide is selected from the group consisting of:

(a) nucleotides 1 to 3094 of SEQ ID NO: 4;

(b) nucleotides 1 to 3718 of SEQ ID NO: 6;

(c) nucleotides 1 to 2801 of SEQ ID NO: 8; and

(d) polynucleotides hybridizing under stringent conditions to (a), (b), or (c).

17. (Amended) ~~[A]~~ The polynucleotide of claim ~~[1]~~ 10, comprising ~~[a nucleotide sequence selected from the group consisting of:]~~

nucleotides 1 to 8388 of SEQ ID NO: 6~~[; and

nucleotides 1 to 7465 of SEQ ID NO: 8]~~.

18. (Amended) The polynucleotide of claim ~~1~~ 7, comprising nucleotides 1 to 8561 of SEQ ID NO: 4.

19. (Amended) The polynucleotide of claim ~~1~~ 4, which is operably linked to a second nucleotide sequence.

21. (Amended) A vector comprising the polynucleotide of claim ~~1~~ 4.

22. (Amended) A host cell containing the polynucleotide of claim ~~1~~ 4.

23. (Amended) An isolated oligonucleotide, comprising at least 15 nucleotides that can hybridize specifically to the polynucleotide of claim ~~1~~ 4, but neither to a polynucleotide encoding SEQ ID NO: 11 nor to a polynucleotide encoding an amino acid sequence consisting of amino acids 1031 to 2517 of SEQ ID NO: 5.

38. (New) A polynucleotide of claim 13, wherein said polynucleotide comprises nucleotides 1 to 7465 of SEQ ID NO: 8.

Please cancel non-elected claims 26-37 without prejudice.

APPENDIX B

Complet set of pending claims

3. (Amended) The polynucleotide of claim 4 and polynucleotides that hybridize thereto under stringent conditions, wherein the SMRT co-repressor comprises a repression domain having

a) less than about 83% identity with a Sin3A interaction domain of N-CoR set forth as amino acids 255 to 312 of SEQ ID NO: 11;

b) less than about 57% identity with repression domain 1 of N-CoR set forth as amino acids 1 to 312 of SEQ ID NO: 11;

c) less than about 66% identity with a SANT domain of N-CoR set forth as amino acids 312 to 668 of SEQ ID NO: 11; or

d) less than about 30% identity with repression domain 2 of N-CoR set forth as amino acids 736 to 1031 of SEQ ID NO: 11.

4. (Amended) An isolated polynucleotide encoding a member of a family of silencing mediators of retinoic acid receptor and thyroid hormone receptor (SMRT), or an isoform or peptide portion thereof (collectively, a SMRT co-repressor), or an isolated polynucleotide complementary thereto, wherein said SMRT co-repressor is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors, and wherein the SMRT co-repressor comprises an amino acid sequence as set forth in SEQ ID NO: 5 or conservative variations thereof.

5. (Amended) An isolated polynucleotide encoding a member of a family of silencing mediators of retinoic acid receptor and thyroid hormone receptor (SMRT), or an isoform or peptide portion thereof (collectively, a SMRT co-repressor), or an isolated polynucleotide complementary thereto, wherein said SMRT co-repressor is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors, and wherein said co-repressor is encoded by a polynucleotide which hybridizes under stringent conditions with SEQ ID NO: 4.

6. (Amended) An isolated polynucleotide encoding a member of a family of silencing m diators of retinoic acid receptor and thyroid hormone receptor (SMRT), or an isoform or peptide portion thereof (collectively, a SMRT co-repressor), or an isolated polynucleotide complementary thereto, wherein said SMRT co-repressor is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors, wherein said co-repressor has at least 80% sequence identity with SEQ ID NO:5.

7. (Reiterated) The polynucleotide of claim 4, which has a nucleotide sequence as set forth in SEQ ID NO: 4, and conservative variations thereof.

9. (Amended) An isolated polynucleotide encoding a member of a family of silencing mediators of retinoic acid receptor and thyroid hormone receptor (SMRT), or an isoform or peptide portion thereof (collectively, a SMRT co-repressor), or an isolated polynucleotide complementary thereto, wherein said SMRT co-repressor is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors, and wherein said polynucleotide encodes a polypeptide having the amino acid sequence set forth in SEQ ID NO: 7 or conservative variations thereof.

10. (Amended) The polynucleotide of claim 9, which has a nucleotide sequence substantially the same as set forth in SEQ ID NO: 6.

12. (Amended) An isolated polynucleotide encoding a member of a family of silencing mediators of retinoic acid receptor and thyroid hormone receptor (SMRT), or an isoform or peptide portion thereof (collectively, a SMRT co-repressor), or an isolated polynucleotide complementary thereto, wherein said SMRT co-repressor is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors, and wherein said polynucleotide encodes a polypeptide having the amino acid sequence set forth in SEQ ID NO: 9 or conservative variations thereof.

13. (Amended) Th polynucleotide of claim 12, which has a nucleotide sequence substantially the same as set forth in SEQ ID NO: 8.

14. (Amended) An isolated polynucleotide encoding a member of a family of silencing mediators of retinoic acid receptor and thyroid hormone receptor (SMRT), or an isoform or peptide portion thereof (collectively, a SMRT co-repressor), or an isolated polynucleotide complementary thereto, wherein said SMRT co-repressor is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors, and wherein said polynucleotide comprises a nucleotide sequence having at least 80% sequence identity with a polynucleotide selected from the group consisting of:

(a) nucleotides 1 to 3094 of SEQ ID NO: 4;

(b) nucleotides 1 to 3718 of SEQ ID NO: 6;

(c) nucleotides 1 to 2801 of SEQ ID NO: 8; and

(d) polynucleotides hybridizing under stringent conditions to (a), (b), or (c),

provided that the polynucleotide does not contain a sequence identical to SEQ ID NO: 11.

16. (Amended) A polynucleotide according to claim 14, wherein said polynucleotide is selected from the group consisting of:

(a) nucleotides 1 to 3094 of SEQ ID NO: 4;

(b) nucleotides 1 to 3718 of SEQ ID NO: 6;

(c) nucleotides 1 to 2801 of SEQ ID NO: 8; and

(d) polynucleotides hybridizing under stringent conditions to (a), (b), or (c).

17. (Amended) The polynucleotide of claim 10, comprising nucleotides 1 to 8388 of SEQ ID NO: 6.

18. (Amended) The polynucleotide of claim 7, comprising nucleotides 1 to 8561 of SEQ ID NO: 4.

19. (Amended) The polynucleotide of claim 4, which is operably linked to a second nucleotide sequenc .

20. (Reiterated) The polynucleotide of claim 19, which encodes a fusion polypeptide comprising the SMRT co-repressor operably linked to a DNA binding domain of a transcription factor.

21. (Amended) A vector comprising the polynucleotide of claim 4.

22. (Amended) A host cell containing the polynucleotide of claim 4.

23. (Amended) An isolated oligonucleotide, comprising at least 15 nucleotides that can hybridize specifically to the polynucleotide of claim 4, but neither to a polynucleotide encoding SEQ ID NO: 11 nor to a polynucleotide encoding an amino acid sequence consisting of amino acids 1031 to 2517 of SEQ ID NO: 5.

24. (Reiterated) The oligonucleotide of claim 23, wherein the polynucleotide encodes at least five contiguous amino acids of a sequence selected from the group consisting of:

amino acids 720 to 745 of SEQ ID NO: 5;

amino acids 716 to 742 of SEQ ID NO: 7; and

amino acids 497 to 523 of SEQ ID NO: 9.

25. (Reiterated) The oligonucleotide of claim 23, which can hybridize specifically to a polynucleotide encoding SEQ ID NO: 5 or SEQ ID NO: 7, but not to a polynucleotide encoding SEQ ID NO: 9.

38. (New) A polynucleotide of claim 13, wherein said polynucleotide comprises nucleotides 1 to 7465 of SEQ ID NO: 8.